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van Eijk, MCP; Bergsma, M; Marrink, SJ

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Association behaviour of glucitol amine gemini surfactants

Self-consistent-field theory and molecular-dynamics simulations

M.C.P. van Eijk[1,a], M. Bergsma[2,b], and S.-J. Marrink[3,c]

[1] Lund University, Center for Chemistry and Chemical Engineering, Physical Chemistry 1, P. O. Box 124, 221 00 Lund, Sweden
[2] University of Groningen, Stratingh Institute, Physical Organic Chemistry Unit, Nijenborgh 4, 9747 AG Groningen, The Netherlands
[3] University of Groningen, Department of Biophysical Chemistry, Nijenborgh 4, 9747 AG Groningen, The Netherlands

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Abstract. The association behaviour of a number of glucitol amine gemini surfactants has been investigated by means of molecular dynamics and self-consistent-field calculations. We have shown that the titratable head group of the surfactant is responsible for a micelle-to-membrane transition when changing the *p*H. Furthermore, the association structure of this group of surfactants is shown to be very sensitive to ionic strength. The combination of a charged head group, a spacer, and the hydrophilic glucitol side chains is responsible for the possible structural transitions in the associates as a function of ionic strength and *p*H.

PACS. 82.70.Uv Surfactants, micellar solutions, vesicles, lamellae, amphiphilic systems (hydrophilic and hydrophobic interactions) – 81.16.Dn Self-assembly – 64.70.Nd Structural transitions in nanoscale materials

1 Introduction

A gemini (or dimeric) surfactant is generally defined as two conventional single-tailed surfactants linked at or near the head group by a spacer [1,2]. Due to the unique properties of these molecules, the interest in gemini surfactants has increased dramatically over the last decade (see Ref. [3] and references therein). The self-association into micelles, bilayers, and other nanoscopic structures is one of the topics which is relevant both to real-life applications as well as to fundamental research. In general, gemini surfactants show a remarkably lower critical micellization (better *association*) concentration (c_0) than their conventional counterparts [4] on a per head group base. One of the areas in which self-association is considered to be important, is the use of cationic surfactants as transfection agents [5]. The use of gemini surfactants would in such case decrease the needed concentration and therefore also reduce the toxic effects which are known for cationic surfactants. Two recent *in vitro* transfection studies show that cationic gemini surfactants indeed are able to efficiently transfer DNA to the cell nucleus [6,7]. Recently, we showed how DNA can be efficiently compacted by different gemini surfactants at extremely low concentrations [8].

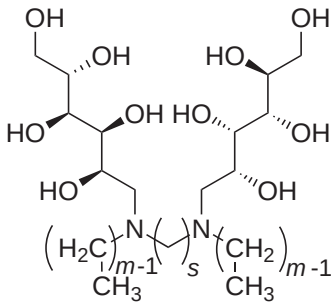

Fig. 1. Molecular structure of the basic form of a family of glucitol amine gemini surfactants as used in references [7,9].

Fielden *et al.* [7] synthesized and used glucitol amine gemini surfactants in their transfection study. Several physico-chemical properties of the same system are reported by Bergsma *et al.* [9]. The molecular structure of the surfactants used in those studies is shown in Figure 1. The sugar residues make the surfactant sufficiently hydrophilic to dissolve to a small extent into water, which is of course essential in biological systems. We have chosen to analyze the association behaviour of these surfactants on a molecular level with simulation techniques in order to understand some of the reported physico-chemical properties.

Although the amount of physico-chemical research related to gemini surfactants is tremendous, theoretical or simulation studies on the remarkable surfactants are still

[a] *Present address*: CP Kelco ApS, Department of Biopolymer Science, Ved Banen 16, 4623 Lille Skensved, Denmark; e-mail: marcel.vaneijk@cpkelco.com
[b] e-mail: bergsma@gmx.net
[c] e-mail: marrink@chem.rug.nl

quite rare. One of the first simulation studies on such systems was carried out by Karaborni *et al.* [10], who studied the association behaviour with molecular dynamics. Maiti and coworkers [11,12] have made some progress in using Monte Carlo simulations in order to describe the association behaviour of some generalized non-ionic gemini surfactants. A third technique which we consider powerful in the study of self-association is the self-consistent-field theory, as used by Leermakers and Scheutjens [13–15] for conventional surfactants.

2 Methods and "materials"

In order to get a detailed picture of the association behaviour of the sugar-based gemini surfactants, we have chosen to use two different simulation techniques. We apply molecular dynamics to obtain structural details about a single membrane forming system and self-consistent-field calculations to look into the effects on associate structure and shape of surfactant architecture and its environment (*e.g.*, *p*H or ionic strength).

2.1 Molecular-dynamics simulation

One way to gather information about the structure of an associate of glucitol amine surfactants is the use of molecular-dynamics (MD) simulations. The microscopic state of a surfactant system of N atoms can be described in terms of the positions ($\mathbf{r}_i$) and momenta ($\mathbf{p}_i$) of the contained atoms. The interactions between the atoms contain both non-bonded (electrostatic and dispersion) and bonded (bond, angle, dihedral) terms. A time trajectory of the system is generated by solving Newton's equations of motion. A time-average of a sufficiently long run corresponds to an ensemble-average.

In the MD simulations the gemini surfactant is built up by connected segments (or "atoms") comparable to atoms in the real surfactant. It should be noted, however, that the CH, CH_2, and CH_3 groups are represented by united atoms, *i.e.*, they are considered as one segment. Furthermore, it is considered that the amine group is unprotonated, implicating a relative high *p*H. All bond lengths and all angles involving hydrogens were constrained using the LINCS algorithm [16]. The interactions are calculated by use of the Gromacs force-field [17], which has proven to be successful in modelling lipid bilayer systems (*i.e.* [18]). The water is modelled as SPC [19]. Its geometry was constrained with the SETTLE [20] algorithm. The constraining algorithms employed are very stable and permit the use of a 5 fs time step [21]. Standard weak-coupling schemes [22] were used to imply the constant pressure (see below) and temperature ($T = 333$ K) conditions. Furthermore, a group-based twin range cut-off scheme was used to treat the non-bonded interactions. A cut-off of 1.0 nm was used for the Lennard-Jones and of 1.5 nm for the electrostatic interactions (updated every 5 time steps). Periodic boundary conditions were applied to generate a quasi-infinite multilamellar system. The system contains 5048 H_2O molecules together with 128 surfactant molecules. Initially, a bilayer was created by placing the lipid molecules on a regular grid. An extensive equilibration procedure (5 ns) ensured the bilayer to adapt an equilibrium configuration. Subsequently, two different 5 ns simulations were performed. In one simulation an isotropic pressure coupling was applied (1 atm in all directions), implying a system with zero surface tension. The other system was subject to a lateral pressure of -100 atm *versus* a perpendicular pressure of 1 atm, implying a small positive surface tension. There is an ongoing discussion in the literature whether or not in small finite systems a small positive surface tension is required to compensate for the tension induced by the suppression of long-wavelength undulatory modes [23,24]. For the current system the effect of the applied surface tension was a small increase in equilibrium area per lipid, 0.82 nm^2 compared to 0.80 nm^2 for the simulation at zero surface tension. Other properties of the bilayer such as the distribution of atom types across the bilayer are almost identical, therefore we will show results obtained for the zero surface tension simulation only (based on the final 2 ns).

2.2 Self-consistent-field theory

The equilibrium behaviour of a surfactant system can be modelled by the use of a mean-field lattice theory in which all molecules in the system are considered to be built up of one or more monomers each occupying one lattice site. We use the self-consistent-field (SCF) formalism developed by Scheutjens and Fleer (SF), which was originally designed for calculations on polymer adsorption [25,26]. The mean-field character of this theory is reflected in the way the properties of the composing molecules are averaged over each layer in the lattice, where the layer boundaries can be either flat, cylindrical or spherical. Leermakers and Scheutjens modified the SF theory for the use on surfactant systems, and also introduced the possibility to account for chain stiffness by the use of a rotational isomeric scheme (RIS) [13]. The SF theory is a combination of two distinct parts. A self-consistent-field part is used to handle the energetic interactions. The electrostatic forces are incorporated in the form of a potential of mean force $u^{\mathrm{el}}(z)$ (used parameters are the relative dielectric permittivity ϵ_i and valency ν_i per monomer) as in the Gouy-Chapman theory, where z is the lattice layer number. Excluded-volume interactions are included in a hard-core potential $u'(z)$ by demanding every layer in the lattice to be filled. Finally, nearest-neighbour interactions are taken into account by the use of an interaction potential $u^{\mathrm{int}}(z)$ (used parameters are the Flory-Huggins interaction parameters χ_{ij} between the different monomers). The second part of the SF approach is the so-called chain-propagation part which accounts for chain connectivity. In its simplest form it uses first-order Markov statistics which basically says that the set of all conformations of a linear molecule of N monomers with the first monomer at position z, can be approximated by by the set of all walks of $N-1$ steps departing from this location. The RIS model is

Table 1. Monomeric parameters for the different monomers in the SCF calculations.

Monomer	ν	pK_a	ϵ
C	0	–	2
NH	+1	8.5	10
OH	0	–	10
Cl	−1	–	10
Na	+1	–	10
H_2O	0	–	80

Table 2. Flory-Huggins χ-parameter between the different monomers in the SCF calculations.

	C	NH	OH	Cl	Na	H_2O
C	0	1.5	1.5	1.5	1.5	1.5
NH	1.5	0	0	0	0	−0.3
OH	1.5	0	0	0	0	−0.3
Cl	1.5	0	0	0	0	−0.3
Na	1.5	0	0	0	0	−0.3
H_2O	1.5	−0.3	−0.3	−0.3	−0.3	0

implemented in the form of third-order Markov statistics. The chain stiffness is characterized by the energy difference Δu^{tg} between the *trans* and *gauche* conformation in a set of three bonds. The pH of the bulk solution is set as an environment variable, so without the explicit addition of protons or hydroxide. As long as $3 < p\mathrm{H} < 11$ and the amount of salt in the system is not too small (typically, a volume fraction $\phi_{\mathrm{b,Na}} > 10^{-4}$), this should be a sufficient description.

The SCF calculations are used to gain information on the association behaviour of the gemini surfactants. In this context it is important to note that the actual system we are investigating is a single surfactant associate with a fixed centre of mass. On this system one can apply thermodynamics of small systems to reveal thermodynamic data on an ensemble of such systems (the macroscopic system). For a general introduction to this method we refer to the original work of Hill [27]. In the context of SCF calculations of surfactant association a detailed description is given by Leermakers and Scheutjens [13–15].

In the SCF calculations the glucitol amine surfactants are coarse-grain-modelled by using three different kind of monomers for the surfactant itself, two for the electrolyte, and one for the solvent (each monomer occupying one lattice site). Table 1 shows the different monomers and their chosen physical parameters. A sample configuration of a gemini surfactant is depicted in Figure 2, where it should be noted that for the sake of simplicity a square lattice is used in contrast to the face-centered-cubic (fcc) lattice in our SCF calculations. The Flory-Huggins interaction parameters between the different monomers are chosen such as to give a rough representation of the sugar-based surfactant. It should, however, be noted that we have not tried to give an exact description of the real system, but that we are able to predict trends in that system. In Table 2 the interaction parameters are displayed. If not stated otherwise, the chain stiffness is characterized by $\Delta u^{\mathrm{tg}} = 1 k_{\mathrm{B}} T$. The volume fraction of Na $\phi_{\mathrm{b,Na}} = 10^{-3}$ if not stated otherwise.

The lattice in the calculations is composed of $M = 40$ parallel layers of thickness $b = 0.15$ nm, where the layers are numbered $i = 1, 2, \ldots, M$. The lattice is furthermore characterized by *a priori* step probabilities λ_{ij}, which give the relative number of contacts of a segment in layer i with those in layer j. Obviously, $\lambda_{ij} = 0$ if $|j - i| > 1$, and $\sum_{j=1}^{M} \lambda_{ij} = 1$. Using this notation every layer i has three values of λ associated to it, *i.e.* λ_0 related to the same layer, $\lambda_{-1}(i)$ related to the previous, and $\lambda_{+1}(i)$ related to the next. The lattice orientation is characterized by λ_0, which is independent of i, whereas λ_{-1} and λ_{+1} depend on the contact area with the previous layer, $A(i-1)$, and that with the next layer, $A(i)$, as follows:

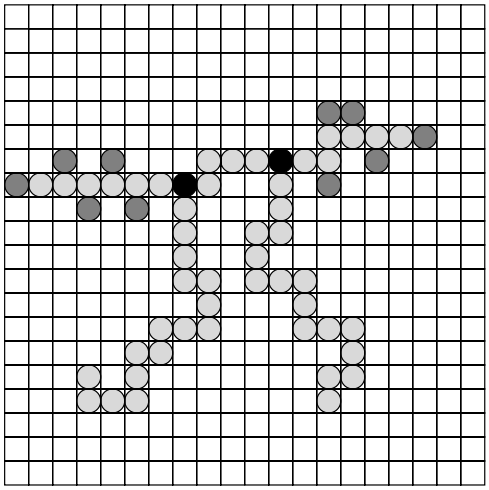

Fig. 2. A sample configuration of the gemini surfactant G16–4–16, on a square lattice, consisting of C (light grey), NH (black), and OH (dark grey) monomers.

$$\lambda_{-1}(i) = \frac{A(i-1)}{A(i-1) + A(i)} \lambda_0, \tag{1}$$

$$\lambda_{+1}(i) = \frac{A(i)}{A(i-1) + A(i)} \lambda_0. \tag{2}$$

The geometry of the lattice can be changed by choosing the appropriate value for $A(i)$:

$$A(i) = \begin{cases} 1 & \text{flat}, \\ 2\pi i & \text{cylindrical}, \\ 4\pi i^2 & \text{spherical}. \end{cases}$$

In all the calculations we use a fcc lattice, characterized by $\lambda_0 = 1/3$.

3 Results and discussion

3.1 Critical association concentration

Before we can make any statement about which kind of associate will be formed by a certain kind of gemini surfactant, it is important to know how to determine the

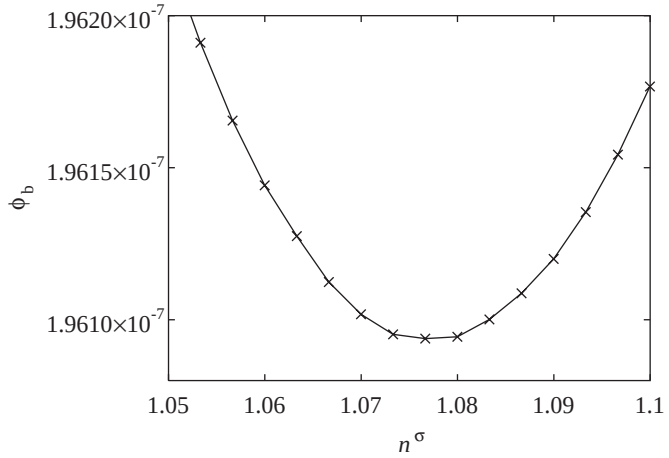

Fig. 3. Bulk volume fraction ϕ_b of gemini surfactant G16–4–16 in a cylindrical geometry as function of excess number of surfactant molecules n^σ at pH = 5.5.

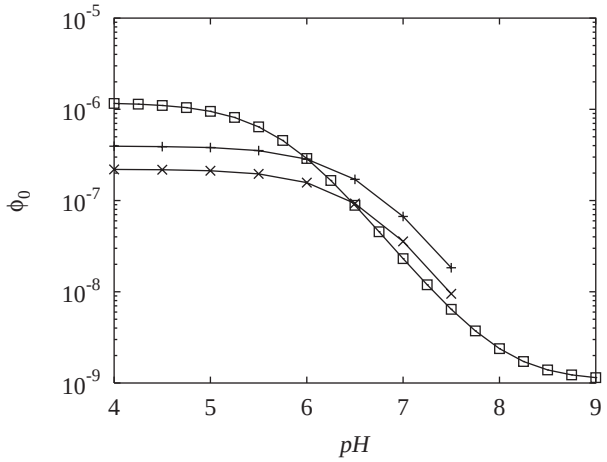

Fig. 4. Critical association volume fraction ϕ_0 for G16–4–16 as a function of pH for three different geometries: (+) spherical, (×) cylindrical, and (□) flat.

so-called critical association concentration (ϕ_0 when considering volume fractions) in the different geometries. Although we are using a mean-field theory, where we average the volume fractions of all monomers in two directions, we can still use three different lattice geometries. This choice enables us to compare lamellar, cylindrical, and spherical surfactant associates in order to determine the most probable shape. For this purpose, we change the total number of surfactants in the system (keeping other parameters constant) and investigate the thermodynamics of the series of systems. As mentioned before, the thermodynamics of small systems [27,13,15] is of use here. As an example, we show in Figure 3 the bulk volume fraction of G16–4–16 in a cylindrical geometry as a function of the excess number of surfactants

$$n^\sigma \equiv \frac{\sum_{i=1}^{M}(\phi(i)-\phi_b)L(i)}{l}, \qquad (3)$$

where $L(i)$ is the volume of layer i in number of lattice sites, l is the number of atoms per surfactant molecule, $\phi(i)$ is the volume fraction of the surfactant in layer i, and ϕ_b is volume fraction of the surfactant in the bulk solution. The minimum in ϕ_b corresponds to the occurrence of the first stable associates [15]. So, this volume fraction equals ϕ_0 for this geometry.

With this knowledge, the most likely shape of the surfactant associate can be deducted by comparing the calculations of the system in question in three different geometries. The geometry with the lowest chemical potential (or lowest bulk volume fraction for that matter) for the surfactant represents the best approximation for the shape of the associate. For G16–4–16 this procedure is illustrated by Figure 4 for different values of pH. One should note that we only compare three ideal shapes, and that intermediate shapes are highly possible. Clearly, a transition from a cylindrical micelle to a lamellar-like structure is observed around pH = 6.5. Fielden *et al.* [7,9] already suggested the existence of this transition for the corresponding real surfactant. They even suggested that such a transition might be of importance for the transfection ability of the surfactant, as long as this transition occurs in the endosomal pH range (4.0–7.4). It is probably not the transition as such which is important though. It is more likely that the change in surfactant charge and shape which causes the transition also is responsible for the change in DNA-surfactant interaction. Especially the increased solubility of the surfactant (reflected in an increased ϕ_0) might play an important role in releasing the DNA if the pH of the environment decreases.

3.2 Monomer distribution in associates

In order to get a detailed picture of the effects of surfactant architecture on the characteristics of the formed associates, it is a good idea to investigate the actual distribution of the composing monomers in the associate. Firstly, we will take a look at a membrane formed by uncharged G16–6–16 as simulated by MD. A graphical snapshot taken from the end of the simulation performed at zero surface tension is presented in Figure 5.

Figure 6 shows the mass fraction profiles across one half of the membrane of the different (united) atoms in the system. A comparable representation of this system from the SCF calculations is given in Figure 7 at pH = 7. As we used a NH group with $pK_a = 8.5$ in the SCF case, the surfactant is partly protonated at pH = 7, but still forms a membrane. Furthermore, volume fractions are used, as all monomers have the same size on a lattice and we did not attribute mass to the different monomers. Despite the differences in the two representations, the actual distribution of the monomers does not differ to a large extent. It should not come as a surprise that the centre of the membrane consists mainly of C monomers. The differences in hydrocarbon content in the centre of the membrane between the MD and the SCF system is, however, a matter of some concern. This discrepancy is caused by a difference in penetration of water into the hydrophobic centre of the

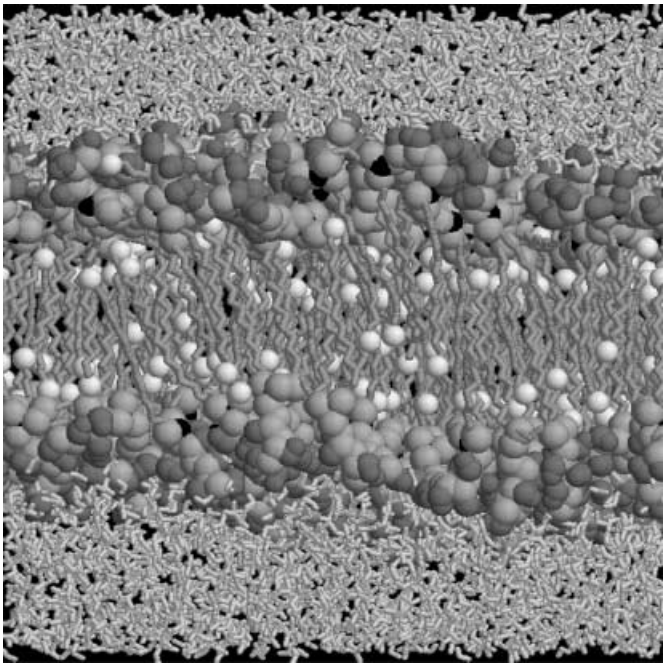

Fig. 5. Snapshot from the end of the MD simulation for the G16–6–16 membrane at zero surface tension. The colouring scheme is the same as for Figure 2. Additionally, the terminal methyl groups are depicted as small white spheres. To highlight the location of the interface all atoms belonging to the lipid head group are also shown as spheres. The water is shown in a light-grey stick representation.

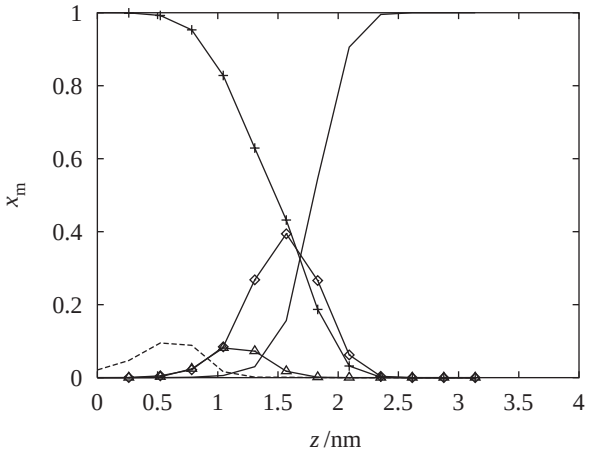

Fig. 6. Mass fraction profiles for the different monomers and groups in G16–6–16 as represented in the MD simulation. (+) C; (△) N; (◇) OH; (dashed line) terminal methyl groups; (solid line) solvent.

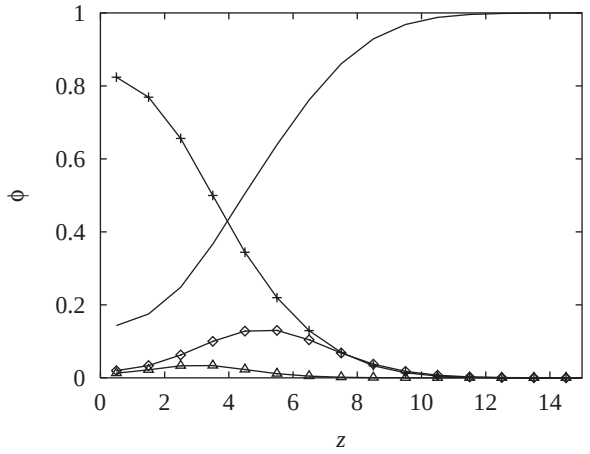

Fig. 7. Volume fraction profiles for the different monomers in G16–6–16 as represented in the SCF calculation in a flat geometry at pH = 7. (+) C; (△) NH; (◇) OH; (solid line) solvent.

membrane. The water content in the SCF case is most likely overestimated due to the fact that water is modelled as a single monomer without the possibility to form hydrogen bridges. In other words, there is no water structure. This makes it relatively easy for water molecules to be present in a hydrophobic environment, as this is now mainly governed by the Flory-Huggins interaction parameter between water and carbon.

Despite the water problem, the position of both the amine and the sugar groups are comparable in the two membranes. From the profiles it is evident that the glucitol groups extend into solution much further than the amine due to their hydrophilic nature.

A further remarkable observation, most clearly visible in the MD simulation, is the interdigitation of the surfactant tails. Both from the snapshot and from the mass fraction profile from the MD results, it is clear that the terminal methyl groups are located away from the centre of the membrane, implying interdigitation. This result is not directly observable in the volume fraction profile from the SCF results, but without interdigitation, the carbon tails would extend much more into the solution than is the case here (only about 9 lattice layers).

A more detailed volume fraction profile at ϕ_0 and pH = 7 for G16–4–16 (different spacer length) is given in Figure 8, where we also make a distinction between C monomers in the tail, spacer and head group (glucitol). In this case we use a logarithmic ϕ-scale to emphasize the details. The amine group and the monomers in the spacer are more or less distributed similarly over the membrane. This is due to the rather short spacer length, making it impossible for the spacer to bend towards the more hydrophobic part of the membrane. Another phenomenon to take notice of is the distribution of the surfactant tails. At a distance of about 12 lattice layers from the centre of the membrane its volume fraction profile shows a distinct change in slope. We speculate that beyond this distance the contribution of free surfactants start to play a role (note the low concentrations).

Another way to look at a surfactant associate is to consider the excess amount of surfactants in the system (*i.e.*, the amount belonging to the associate). If one does this in a cumulative fashion in the SCF approach one can actually get an idea of the actual size of the associate. The

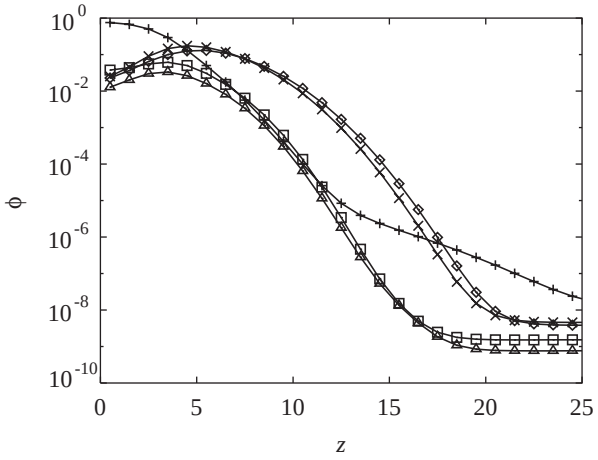

Fig. 8. Volume fraction profiles for the different monomers in G16–4–16 at pH = 7. (+) C_{tail}, (×) C_{head}, (□) C_{spacer}, (△) NH, and (◇) OH.

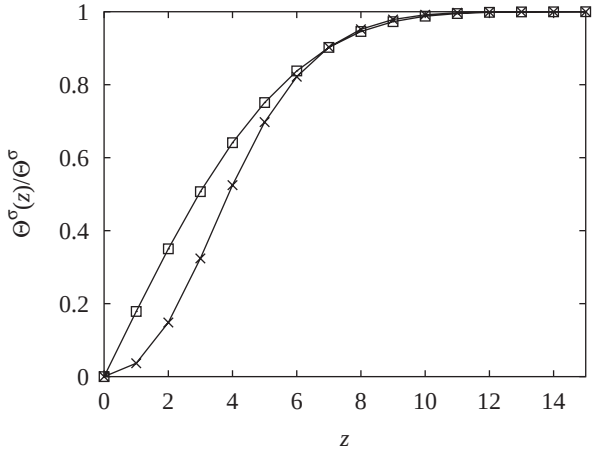

Fig. 9. Cumulative relative volume fraction profiles for G16–4–16 at pH = 6.5 close to the transition from cylindrical to lamellar associates. Geometries: (×) cylindrical and (□) flat.

excess amount up to layer z of the surfactant is defined as

$$\Theta^\sigma(z) \equiv \sum_{i=1}^{z} (\phi(i) - \phi_b) L(i), \tag{4}$$

where $L(i)$ is the volume of layer i in number of lattice sites (compare with Eq. (3)). Figure 9 shows this quantity for G16–4–16 close to the micelle-membrane transition for the two geometries. Although the membrane structure is denser in the centre than the micelle, they extend almost equally far into the bulk solution. To give an idea about the size of the associate, we plot the number of layers z_{95} from the centre of the associate within which 95% of the excess amount of surfactant can be found in Figure 10.

In analyzing the size of the associate as a function of pH it is good to realize that the amine groups are completely protonated at pH = 4, whereas they are deprotonated at pH = 9. It is interesting to note that if one forces the surfactants into a cylindrical geometry, the size of the formed associated does hardly change with pH,

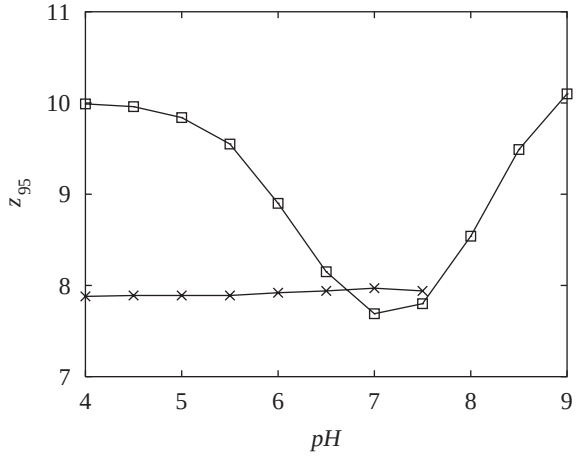

Fig. 10. Associate size of G16–4–16 as a function of pH expressed in terms of z_{95} (95% of the excess amount of surfactant within this distance). Geometries: (×) cylindrical and (□) flat.

whereas in the membrane case a size change of approximately 20% can be observed. For the fully protonated surfactants, the spacer is completely extended due the repulsion between the amine groups within the same surfactant. The high charge also causes a repulsion between the surfactants. This effect promotes a cylindrical micellar structure where the hydrophobic tails can be confined in a relatively small volume, whereas the repulsion between the amine groups increases the curvature of the associate. In a cylindrical geometry the glucitol groups can gain conformational entropy by adapting a non-extended conformation on the outside of the associate. If one, however, forced the molecules in a membrane structure,there would be no possibility to confine the hydrophobic tails in a small volume, because of the repulsion of the charged amine groups. The structure of such a membrane would therefore be less compact and would extend much further into solution. At intermediate pH, the membrane structure is compacted due to decreased repulsion and confining the tails in a smaller volume. The cylindrical associate would not change too much, because of the volume restrictions for the tails. A further decrease of protonation leads to an extension of the glucitol groups into solution and thus increases the associate size. For the membrane case this also means that one is able to pack more surfactants per unit area into the membrane as is shown in Figure 11.

3.3 Effects of spacer length and ionic strength

So far we discussed the effect of the environment on the association behaviour of the gemini surfactants. Another way to influence this behaviour is by changing the architecture of the surfactant. Here, we have chosen to take a closer look at the effects of spacer length on the association behaviour. Figure 12 shows the critical association volume fraction at different values of pH for G16–s–16 as a function of spacer length. We clearly observe a decrease of ϕ_0 as a function of s. It is well known from regular surfactants that the addition of C monomers to a surfactant

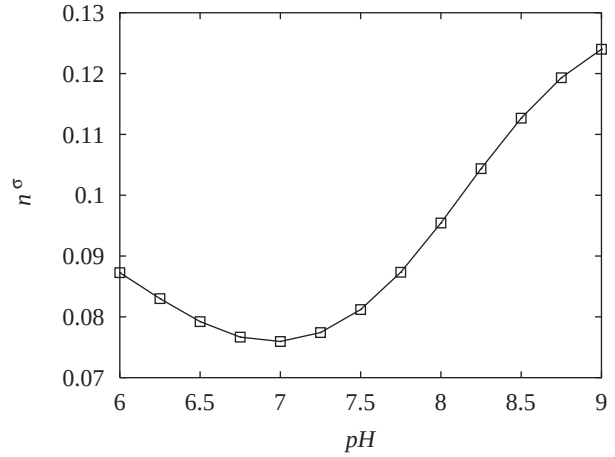

Fig. 11. Excess number of surfactant molecules per unit area for G16–4–16 in a flat geometry as a function of *p*H.

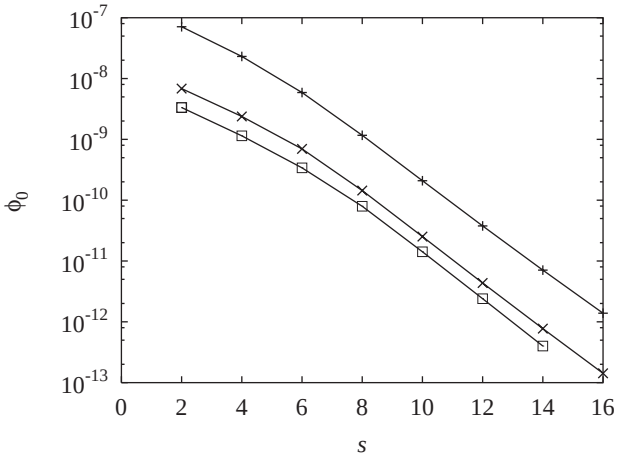

Fig. 12. Critical association volume fraction for G16–*s*–16 (gemini surfactants with different spacer lengths) in a flat geometry at different values of *p*H. (+) *p*H = 7, (×) *p*H = 8, and (□) *p*H = 9.

tail increases its hydrophobicity and this will subsequently lead to decrease of ϕ_0 according to

$$-\log \phi_0 \propto m + \text{const}, \tag{5}$$

where m is the tail length. In our case, however, the C monomers are added to the spacer, where we still expect the same effect if the spacer can reside in the hydrophobic part of the associate, implying large s. This seems indeed to be the case. On close inspection of the curves in Figure 12 one observes a change in slope around $s = 6$. For $s > 8$ equation (5) is clearly obeyed (replacing m by s, of course). Below this value the spacer becomes more or less rigid and is forced to be on the outside of the associate. If the glucitol groups had not been present, this might have even led to a maximum in ϕ_0 as is, *e.g.*, observed for gemini surfactants of type $(C_mH_{2m+1}N^+Br^-)_2(CH_2)_s$ [28,4]. Due to the very low critical association concentration of the glucitol amine surfactant, also reflected in the formation of vesicles [9], no experimental cmc data is available for the present system.

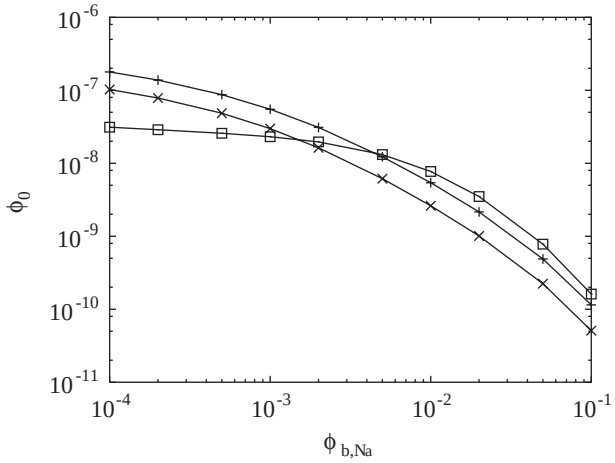

Fig. 13. Critical association volume fraction for G16–4–16 as a function of salt concentration at *p*H = 7 in different geometries: (+) spherical, (×) cylindrical, and (□) flat.

Instead of changing the *p*H to change the electrostatic interactions, one can also change the ionic strength of the solution by adding salt to the solution. Addition of salt to the system will screen the electrostatic interactions, which is especially of interest when considering the head group conformation. As one expects this conformation to change with ionic strength, it is also likely that the preferred associate structure might change as well. From Figure 4 one sees that for G16–4–16 at $\phi_{b,Na} = 10^{-3}$ and *p*H = 7 the system is close to the micelle-membrane transition. It is therefore likely that small changes in ionic strength might bring about that transition. In Figure 13 we display the ϕ_0 for G16–4–16 in the different geometries as a function of the amount of added salt. Two observations can be made about this dependency. Firstly, a decrease of the critical association volume fraction occurs with increasing ionic strength. This phenomenon is simply related to the increasing non-ionic nature of the surfactant due to screening of the charges, decreasing the solubility of the gemini surfactant. Secondly, and more importantly, at low salt concentrations the effect of the screening on ϕ_0 is much smaller in the membrane case than in the micelle case. This odd behaviour introduces a membrane-micelle transition with *increasing* ionic strength, whereas one intuitively would expect the opposite. The key clue here is the presence of the glucitol groups connected to the charged amine. One should also remember that the amine groups are not fully protonated at this *p*H. At low ionic strength the spacer is slightly stretched and the glucitol groups have enough conformational freedom in a membrane structure, while at the same time the tails are allowed to pack to a certain extent. Increasing the ionic strength favours the latter effect, but this enthalpic favour cannot compensate for the loss of entropy of the glucitol groups, which are now forced to extend into solutions. However, they gain entropy again when the surfactants form a cylindrical micelle, which is what happens. This behaviour is clearly reflected in the size of the associates as can be seen in Figure 14.

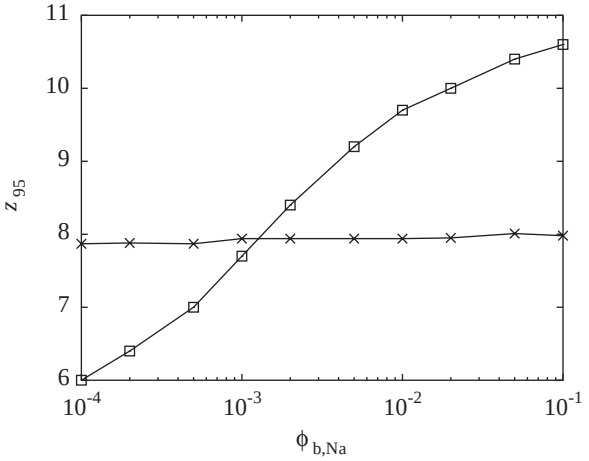

Fig. 14. Associate size of G16–4–16 as a function of salt concentration (in terms of z_{95} as used in Fig. 10). Geometries: (×) cylindrical and (□) flat.

4 Conclusions

The association behaviour of glucitol amine gemini surfactants is more complicated than one might expect on first sight. The conformational flexibility caused by a rather flexible spacer and two hydrophilic sugar residues attached to the cationic head group, makes it possible to adapt quite different associate structures depending on its environment. One of the key findings is that the G16–*s*–16 surfactants at intermediate ionic strength undergoes a cylindrical micelle-membrane transition in the endosomal *p*H range (4.0–7.4), which is considered to be of importance when the surfactant is to be used as a synthetic vector in gene transfection. This transition is related to the fact that the glucitol "chains" essentially give the surfactant a flexible head group, which can compensate for unfavourable electrostatic interactions between the amine head groups (both inter- and intramolecular).

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